ACUTE TOXICITY SUMMARY

METHYL CHLOROFORM

(1,1,1-trichloroethane, methyltrichloromethane)

CAS Registry Number: 71-55-6

I. Acute Toxicity Summary (for a 1-hour exposure)

Inhalation reference exposure level	**68,000 µg/m³**
Critical effect(s)	subtle impairment of the central nervous system
Hazard Index target(s)	Nervous System

II. Physical and Chemical Properties (HSDB, 1994 except as noted)

Description	colorless liquid
Molecular formula	$C_2H_3Cl_3$
Molecular weight	133.42
Density	1.3376 g/cm^3 @ 20°C
Boiling point	74.1°C
Melting point	-30.4°C
Vapor pressure	127 mm Hg @ 25°C
Flashpoint	not applicable
Explosive limits	upper = 10.5% lower = 8.0%
Solubility	soluble in acetone, benzene, methanol, carbon tetrachloride
Odor threshold	390 ppm (geometric mean) (AIHA, 1989)
Odor description	sweet, chloroform-like odor
Metabolites	trichloroethanol, trichloroacetic acid (ACGIH, 1991)
Conversion factor	1 ppm = 5.46 mg/m³ @ 25°C

III. Major Uses or Sources

Methyl chloroform is used as a solvent for adhesives and for metal degreasing (ACGIH, 1991). It is also used in the manufacture of vinylidene chloride. Methyl chloroform is also used in textile processing and dry cleaning.

IV. Acute Toxicity to Humans

Cardiac arrhythmia resulting from heightened cardiac sensitivity to epinephrine has been reported in several case reports of high acute inhalation exposures to methyl chloroform (ATSDR, 1990). There are case reports of arrhythmias persisting for two weeks or more after cessation of exposure to methyl chloroform (McLeod *et al*., 1987).

Twelve human volunteers were exposed to 250, 350, 450, and 550 ppm (1,400, 1,900, 2,500, and 3,000 mg/m³) methyl chloroform sequentially for 30-minutes per concentration for a total of 2 hours (Gamberale and Hultengren, 1973). Tests to measure manual dexterity, perceptual speed, and reaction time were administered during each of the four exposures. No adverse effects were observed during a 30-minute exposure to 250 ppm (1,400 mg/m³) methyl chloroform. A statistically significant reduction in task performance was observed during the subsequent 30-minute exposure to 350 ppm (1,900 mg/m³) methyl chloroform.

Equilibrium and coordination were impaired as indicated by an abnormal Romberg test and an abnormal Flannagan Aptitude Classification test (a test of coordination) in three of four human subjects exposed to 920 ppm (5,000 mg/m³) methyl chloroform for 70-75 minutes (Torkelson *et al*., 1958). Slight eye irritation and light-headedness were reported by the subjects.

Six male volunteers were exposed to 35 and 350 ppm (190 and 1,900 mg/m³) methyl chloroform for 6 hours on two separate occasions (Nolan *et al*., 1984). Absorption was determined to be 25% of the inhaled dose. Of the absorbed dose, 91% was excreted unchanged in the expired air. Although the odor was perceptible for the duration of the exposure, no subjective symptoms were reported by the volunteers.

Transient eye irritation was reported in 3 of 6 human volunteers exposed to a mean concentration of 500 ppm (3,000 mg/m³) methyl chloroform for 78 minutes (Stewart *et al*., 1961).

Predisposing Conditions for Methyl Chloroform Toxicity

Medical: Persons with preexisting eye, skin, respiratory, liver or cardiovascular disease may have increased sensitivity. Those persons using epinephrine-containing bronchodilators may be at greater risk of developing cardiac arrhythmias when exposed to methyl chloroform (Reprotext, 1999).

Chemical: Alcohol use concurrent with methyl chloroform exposure has been shown to potentiate methyl chloroform toxicity in rats (Reprotext, 1999).

V. Acute Toxicity to Laboratory Animals

A 1-hour LC_{50} of 18,400 ppm (1×10^5 mg/m³) methyl chloroform was reported in mice (Moser and Balster, 1985). A separate study exposed mice continuously to 13,500 ppm (7.4×10^4 mg/m³) methyl chloroform (Gehring, 1968). The onset of anesthesia and death were noted as a function of time. The duration of exposure responsible for the onset of anesthetic effects in 50% of the test population (ET_{50}) is reported as 16.3 minutes. The duration of exposure lethal to 50% of the test population (LT_{50}) is reported as 595 minutes.

Heightened cardiac sensitivity to epinephrine following exposure to methyl chloroform has been observed in dogs (Rennick *et al*., 1949). Sensitivity to methyl chloroform induced arrhythmias

was not found to be greater in dogs with experimentally induced myocardial infarctions (Trochimowicz *et al*., 1976).

A dose-related increase in response time on a discrimination task was observed in 4 baboons exposed to 1,400, 1,800, or 2,100 ppm (7,600, 9,800, or 11,000 mg/m^3) methyl chloroform for 4 hours (Geller *et al*., 1982). No effect on response time was noted following a 4-hour exposure to 700 ppm (4,000 mg/m^3) methyl chloroform.

VI. Reproductive or Developmental Toxicity

No human reproductive studies were located in the literature (Reprotext, 1999). Pregnant rats were exposed to 2,100 ppm (11,000 mg/m^3) methyl chloroform 6 hours per day on days 1-20 of gestation (York *et al*., 1982). Decreased fetal body weight and a significant increase in skeletal and soft tissue variation were observed. No lasting developmental effects were observed as measured by body weight and neurobehavioral tests during postnatal evaluation.

No significant adverse reproductive or developmental effects were observed following the exposure of pregnant rats and mice to 875 ppm (4,780 mg/m^3) methyl chloroform 7 hours per day on days 6 through 15 of gestation (Schwetz *et al*., 1975).

VII. Derivation of Acute Reference Exposure Level and Other Severity Levels (for a 1-hour exposure)

Reference Exposure Level (protective against mild adverse effects): 68,000 μg/m^3

Study	Gamberale and Hultengren, 1973
Study population	twelve human volunteers
Exposure method	inhalation of methyl chloroform
Critical effects	reduced performance in manual dexterity, perceptual speed, and reaction time
LOAEL	350 ppm
NOAEL	250 ppm
Exposure duration	30-minutes (see Table 12 for information on "n")
Extrapolated 1 hour concentration	125 ppm (250^1ppm * 0.5 h = C^1 * 1 h)
LOAEL uncertainty factor	1
Interspecies uncertainty factor	1
Intraspecies uncertainty factor	10
Cumulative uncertainty factor	10
Reference Exposure Level	12.5 ppm (68 mg/m^3; 68,000 μg/m^3)

Level Protective Against Severe Adverse Effects

No recommendation is made due to the limitations of the database.

Level Protective Against Life-threatening Effects

NIOSH (1995) lists an IDLH of 700 ppm. An abnormal Romberg test was observed in one of three human volunteers exposed to 900 ppm (5,000 mg/m³) methyl chloroform for 20 minutes (Stewart *et al*., 1961). Two of three subjects reported lightheadedness. In another study, equilibrium and coordination were impaired in three of four human subjects exposed to 920 ppm (5,000 mg/m³) methyl chloroform for 70-75 minutes (Torkelson *et al*., 1958). Slight eye irritation and light-headedness were reported by the subjects. Although incoordination and loss of equilibrium are non-lethal effects, the NIOSH-IDLH uses these endpoints because such effects could be potentially lethal in the workplace. Thus, the level protective against life-threatening effects is 700 ppm. This level should be re-evaluated when better data become available.

VIII. References

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(ACGIH) American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Cincinnati (OH): ACGIH; 1991. p. 958-964.

(AIHA) American Industrial Hygiene Association. Odor thresholds for chemicals with established health standards. Akron (OH): AIHA; 1989. p. 23.

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